TOBACCO INDUSTRY RESEARCH COMMITTEE

CONFIDENTIAL

TIRC Grant #89 Progress Report #1

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Individual Patterns of Circulatory Response to Cigarette Smoking: Ballistocardiographic Studies

Since the orignal application to the Tobacco Industry Research Committee a year ago for assistance in a project concerning individual patterns of circulatory response to cigarette smoking, the basis of our collaboration has been broadened to include other objectives and the support we have received has been of two kinds. First, a research grant of $4,000 has supplemented funds received from the National Institutes of Health for grant H-1891(c) entitled "A Study of the Precursors of Hypertension and Coronary Artery Disease". The grant from the Tobacco Industry Research Committee has provided the salaries of a part-time Fellow, Dr. Amirali Kassam, and of two clerical assistants. It has also covered most of the running expenses incurred while carrying out ballistocardiographic smoking tests on the Johns Hopkins medical students during the current academic year. Secondly, our need for continuing counsel and advice concerning the statistical aspects of the combined study has been met by the assignment of Miss Mary Burke, the Statistician of the Tobacco Industry Research Committee, to our project three days a week.

The work resulting from this support by the Committee is as follows:

1. Physiologic studies on the effects of smoking.

A. The first paper dealing with the ballistocardiographic smoking test, entitled "Observations on the Individual Effects of Smoking on the Blood Pressure, Heart Rate, Stroke Volume and Cardiac Output of Healthy Young Adults" was submitted for publication in December and is to appear in the May issue of the Annals of Internal Medicine. Although work on this paper was essentially complete in October, several conferences with Miss Burke were most helpful in the final orientation of the statistical findings to the paper as a whole. A brief summary of the results to be published in this paper is given in the Progress Report for 1955-1956 to the National Institutes of Health. (See Appendix A)

B. The effect of smoking upon certain other ballistocardiographic measurements has been studies with the assistance of Dr. Kassam. Using the same 113 smoking tests, the JK/IJ ratio and the ratio between the small (S) and large (L) IJ waves, which occur in expiration and inspiration respectively, have been analyzed. The findings are given in Appendix B, Tables I and II.

1. It will be seen that smoking produced no substantial change in most of these ratios, either when the group as a whole is considered or when the group is subdivided according to a) sex, b) smoking habits or c) parental history of hypertension or coronary artery disease. The only statistically significant changes are indicated in Tables I and II, Appendix B.

2. In particular, there was no significant difference between smokers and nonsmokers in the effect of smoking on the JK/IJ ratio.

3. The smokers, who had the higher $IJ_S / IJ_L \times 100$ ratio, showed a significant decrease after smoking, while the nonsmokers did not. It is possible

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that this finding may reflect an alteration in the respiratory pattern associated with the inhalation of tobacco smoke.

4. The women showed the most pronounced deepening of the K wave after smoking of any group, while the subjects with hypertensive parental history showed a decrease in the size of the K wave after smoking.

5. The offspring of hypertensive parents had the largest mean value (1.15) for the JK/IJ ratio during the control period, indicating that the K waves were most prominent in that group. It is know that deep K waves are characteristic of the hypertensive patient. Our finding is of interest, therefore, because it suggests that the ballistic pattern characterized by deep K waves may precede the onset of elevated blood pressure.

C. Studies concerning the effect of smoking on the ballistocardiographic form of healthy young adults.

1. The first 225 smoking tests carried out on medical students 21-35 years of age have been reviewed in regard to the normality of ballistocardiographic form. Of this number, 18 subjects, or 8 percent showed borderline or early abnormal changes. (Table I, Appendix C) In three individuals such changes were present before smoking; one of these deteriorated further after the first cigarette. In thirteen subjects normal form in the control tracing became borderline or abnormal after the first cigarette. In two, these changes followed the second cigarette.

2. The borderline changes in ballistocardiographic form consisted chiefly of rounding, blunting or notching of the J and K waves and the occasional presence of early M waves in successive cycles. In the records interpreted as "abnormal", these changes were somewhat more pronounced, the small complexes had decreased in size and become somewhat irregular. In two individuals the record was distorted by tumultuous action with exaggerated waves during tachycardia after smoking. In all but two records (indicated by asterisks in Table I, Appendix C) the abnormal form was slight enough to permit measurement of the complexes.

3. Certain characteristics of the 18 subjects with alterations in ballistocardiographic form have been summarized in Tables I and II, Appendix C. In comparison with an unselected total population of subjects, these 18 subjects show (Table III, Appendix C):

a. A higher proportion of smokers and former smokers.
b. A smaller proportion of nonsmokers.
c. A higher proportion of parental hypertension and/or coronary artery disease.
d. A higher mean blood cholesterol level.
e. A higher proportion of individuals who are more than 20 pounds overweight.

In addition to these differences, the mesomorphic build was present in most of the 18 subjects under consideration. The incidence of mesomorphy is undoubtedly much higher than that found among the medical students as a whole, but we have not yet analyzed our general data in this regard.

In summary, the 18 subjects with ballistocardiographic changes are somewhat different from their classmates in a number of ways. The traits which characterize them are those which are thought to be commonly associated with coronary artery disease,

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namely, family history of cardiovascular disease, elevated blood cholesterol levels, mesomorphy and obesity. The majority of the 18 have been smokers for a period of years. Our present data does not allow us to do more than point out the associations. We do not yet know the cause of the deterioration of the ballistocardiographic form in these individuals.

D. Studies on the effect of smoking on the same individual at different times of day and on different days are in progress. The design of the experiment is as follows: the participants are all smokers in the class of 1958. The subject comes to the laboratory at eight in the morning, before breakfast and before smoking, and a one-cigarette smoking test is performed. On the same day the subject has another such test at one o'clock, after morning classes and before lunch. The subjects are allowed to smoke if they please up to noon; if they have smoked, the number of cigarettes is recorded. The two tests are performed by the same examiner. Later in the year the student returns for two more smoking tests on the same day, one before breakfast and one before lunch, as before. In this way each subject has four smoking tests on two days at two different times of day. Twenty-six subjects have completed the first two tests, and we are in process of repeating the tests for the second half of the study.

II Compilation of Data

A. The following portions of the combined study are in the process of being coded for IBM punch cards:

1. Card 1. General information
   a. Study identification number; other identifying material.
   b. Age; sex; birthplace; ancestry
   c. Parental history of hypertension, coronary artery disease, obesity and diabetes.
   d. Summary of smoking habits.
   e. Percentage of over-or underweight.
   f. Status of subject at time of Rorschach test
   g. Total number of responses to Rorschach test
   h. Summary of academic standing.

2. Card 2. Studies of blood pressure and heart rate.
   a. Under resting conditions.
   b. As affected by the cold pressor test.
   c. As affected by the double Master exercise test.
   d. As affected by the anoxemia test.
   e. As affected by the smoking test.

3. Card 3. Analysis of smoking habits.

4. Card 4. Analysis of cholesterol data

5. Card 5. Analysis of the Rorschach data

6. Card 6. Analysis of other habit survey data

7. Card 7. Analysis of other physiologic data

The first set of cards has been completed and frequency distribution tables and crosscorrelations between various items are now being analyzed.

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Appendix A

A. During the current year we have:

1. Continued to collect genetic, physiologic, phychologic and metabolic data on the Johns Hopkins medical students. Microfilemed data from 1954-1955.

2. Sent out five-year follow-up questionnaires to the class of 1951, the fourth class thus studied.

3. Completed a paper concerned with smoking tests given on the ballistocardiograph. (See publications sheet) Statistically significant changes occurred in systolic pressure, diastolic pressure, pulse pressure, heart rate, stroke volume, cardiac output and cardiac index after smoking once cigarette. The direction and degree of change after smoking varied greatly from subject to subject, so that striking individual differences in circulatory patterns were found. On the average, students with parental hypertension, whose control cardiac output and cardiac index were large to begin with, showed more than twice as great an increase in cardiac output and cardiac index as did subjects with negative parents. Likewise, subjects with a parental history of coronary artery disease showed very little increase in cardiac output and cardiac index in contrast to subjects with negative parents.

4. Completed the statistical analysis of cholesterol data on 612 subjects, with particular regard to sources of variation such as age and sex of subject, and the reliability of laboratory method. This basic paper is now being written.

5. Analyzed the relationship of parental history to the total blood cholesterol of the subject. This paper is to appear as a companion to, or immediately after, the previous one. (See 4)

6. Completed plans for tabulation of the study as a whole on IBM cards and taken first steps to set this process in motion.

7. Received a supplementary grant of $4,000 from the American Tobacco Industry Research Committee on October 1, 1955, which has enabled us to carry out duplicate smoking tests on the class of 1958 with the assistance of a part-time Fellow, and to obtain additional clerical assistance for the tabulation of the data on smoking habits of more than 800 subjects for analysis and cross-correlation with other aspects of the study.

B. The Tobacco Industry Research Committee has loaned us their statistician, Miss Mary Burke, three days a week since the beginning of October, as a consultant. This temporary addition to our staff has been most valuable.

C. Mrs. Bernice H. Cohen is associated with the study part-time this year while continuing her studies for a Ph.D. degree in Human Genetics, under a Predoctoral Fellowship from the National Institutes of Health.

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		JK/IJ Ratio					IJ_S/IJ_L X 100 Ratio				
		Total	Men	Women	Smokers	Nonsmokers	Total	Men	Women	Smokers	Nonsmokers
Number of subjects		113	103	10	81	32	113	103	10	81	32
Control Values	Mean	1.11	1.11	1.09 [A]	1.11	1.12	72	72	74	74 [B,C]	68 [C]
	Lowest	0.88	0.88	0.91	0.91	0.88	45	45	50	52	45
	Highest	1.40	1.40	1.24	1.40	1.36	96	89	96	96	87
After First Cigarette	Mean	1.11	1.11	1.17 [A]	1.11	1.13	70	70	69	70 [B]	69
	Lowest	0.92	0.92	1.06	0.92	0.93	47	47	47	52	47
	Highest	1.52	1.52	1 .27	1.50	1.52	84	84	81	84	83
After Second Cigarette	Mean	1.12 [1]	1.11 [2]	1.17	1.12 [3]	1.12	70 [1]	70 [2]	72	70 [3]	70
	Lowest	0.77 [1]	0.77 [2]	1.03	0.77 [3]	1.02	43 [1]	43 [2]	43	49 [3]	43
	Highest	1.54 [1]	1.54 [2]	1 .30	1.54 [3]	1.50	97 [1]	91 [2]	97	97 [3]	83

1 Out of 113, 110 had second sigarette test.

2 Out of 103, 100 men had second cigarette test.

3 Out of 81, 78 had s econd cigarette test.

Statistically significant comparisons:

a. Change with smoking $p < .01$

b. Change with smoking $p < .01$

c. Difference between smokers and nonsmokers $p < .01$

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TABLE II

		JK/IJ Ratio				IJ_S/IJ_L X 100 Ratio			
		H-C-	H+C-	H-C+	H+C+	H-C-	H+C-	H-C+	H+C+
Number of Subjects		49	12	11	9	49	12	11	9
Control Values	Mean	1.11	1.15 A	1.12	1.09	73	72	74	70
	Lowest	0.88	1.07	0.98	1.03	53	50	58	52
	Highest	1.36	1.21	1.25	1.18	96	87	86	83
After First Cigarette	Mean	1.13	1.08 A	1.14	1.10	71	70	71	68
	Lowest	0.93	0.95	1.00	0.97	52	47	53	56
	Highest	1.52	1.19	1.36	1.24	83	82	87	75
After Second Cigarette	Mean	1.12 [1]	1.12 [2]	1.14	1.12	72 [1]	68 [2]	68	69
	Lowest	0.77 [1]	0.95 [2]	0.93	1.00	49 [1]	43 [2]	58	52
	Highest	1.50 [1]	1.21 [2]	1.40	1.23	97 [1]	81 [2]	81	79

[1] Out of 49, 47 had second cigarette test.

[2] Out of 12, 11 had second cigarette test.

Statistically significant comparisons:

a. Change with smoking $p < .01$

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TABLE II

Appendix C

Age, Sex and Smoking Habits of Eighteen Subjects showing Borderline or Abnormal Ballistocardiographic Form

Subject No.	Sex	Age	BCG Form: Control	BCG Form: After 1st Cigarette	BCG Form: After 2nd Cigarette	Smoking Habits	Years of Smoking	Amount Smoked Daily: Cigarettes	Amount Smoked Daily: Pipes	Amount Smoked Daily: Cigars	Remarks
55204	F	28	A	A	A	S	8	10	0	0	Vomited after 2nd cigarette
53137	M	28	B	A	A	S	10	15	0	0	
53162	M	28	B	B	B	S	12	30	0	0	
58119	M	32	N	A*	-**	S/N	8	20/0	0	0	Nausea, pallor, sweating and weakness after 1st cigarette
58174	M	22	N	A	A	S		20-40	+	+	Smokes chiefly on weekends
57134	M	23	N	A*	A*	S	4	12-15	0	0	Marked tachycardia
53128	M	27	N	A	B	S	8	15	0	0	
58148	M	22	N	B	A	N	0	0	0	0	
58114	M	22	N	B	B	N	0	0	0	0	
56151	M	23	N	B	B	S	7	20	0	1-2	
53176	M	26	N	B	B	S	8	30	0	0	
56160	M	23	N	B	B	S	7	0	12	0	
58169	M	23	N	B	B	S/Occ.	½/6	+/Occ.	+/0	0	
56211	F	27	N	B	B	S		10	0	0	
58238	F	23	N	B	B	S/N	5	20/0	0	0	
53123	M	29	N	B	B	S/Occ.	½/10	20/Occ.	0	0	
53108	M	25	N	N	A	S	5	0	4-5	1	
53142	M	26	N	N	B	S	5	0	+	0	

N equals normal form
B equals borderline, abnormal form
A equals abnormal form
* equals could not be measured
** equals test discontinued

S equals Smoker
N equals Nonsmoker
Occ. equals occasional smoker
S/N equals now nonsmoker, previously smoker
+ equals smokes, amount unspecified

Source: https://www.industrydocuments.ucsf.edu/docs/mzll0060

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TABLE II

Other Characteristics of Eighteen Subjects showing Borderline or Abnormal Form

Subject No.	Sex	Age	First Cholesterol	Parental H/C	Height	Weight	Pounds Overweight
55204	F	28	160	+	69	173	+ 24
53137	M	28	330	+	75	20	+ 13
53162	M	28	295	-	74	193	+ 11
58119	M	32	244	-	67	136	-13
58174	M	22	265	*	71	227	+69
57134	M	23	250	*	73	174	+ 5
53128	M	27	360	+	72	181	+ 12
58148	M	22	310	*	67	152	+ 10
58114	M	22	266	+	69	183	+ 33
56151	M	23	298	+	69	174	+ 23
53176	M	26	288	+	74	162	-18
56160	M	23	207	?	72	208	+ 44
58169	M	23	203	*	74	162	-13
56211	F	27	222	-	68	117	-28
58238	F	23	222	+	65	130	0
53123	M	29	185	+	73	230	+53
53108	M	25	243	-	73	291	+118
53142	M	26	258	+	71	173	+ 10

* equals neither parent over 50 years old
H/C equals hypertension and/or coronary artery disease

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Appendix C

TABLE III

Characteristic	18 subjects with changes in BCG form	Unselected Subjects	
			N
Regular smoker	67%	50%	260
Nonsmoker	11%	32%	260
Mean cholesterol level (in mgm s. percent)	256	229	612
Parental history of hypertension and/or coronary artery disease	50%	28%	260
Overweight by 20 lbs. or more	39%	12%	257

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Source: https://www.industrydocuments.ucsf.edu/docs/mzkl0000